CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74726

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

I returned a call from Michael Poirier and confirmed we had received a 8/20/98 amendment to application. He wished to know if the application was now ready for approval.

I explained that we had logged the 8/20/98 piece as a bioequivalence amendment. I referred him to our Tentative Approval letter of 3/6/97. I asked that he submit a formal response to that letter as a Minor Amendment. He should certify that there have been no changes to the application (aside from the revised dissolution specifications which have been agreed to by our Div. Of Bioequivalence) if that is the case (or provide information on any other changes, i.e., in labeling, etc.). I said he should reference the 2/13/98 piece which provides evidence that the Paragraph 4 court case was dismissed and the 8/20/98 piece which provides revised finished product specifications which the chemist will need to review.
He thanked me for the information and this concluded the conversation.

DATE
8/28/98

APPLICATION NUMBER
74-726

TELECON

INITIATED BY APPLICANT

PRODUCT NAME
Potassium Chloride Extended-release Tablets

FIRM NAME
Upsher-Smith

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Michael Poirier

TELEPHONE NUMBER
612-473-4412

SIGNATURE
/S/

(635)

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room N461

From: **Division of** Office of Generic Drugs **HFD-** 613
Attention: Labeling Review Branch **Phone:** 5940367

Date:

Subject: Request for Assessment of a Trademark for a Proposed New Drug Product

Proposed Trademark: KLOR-CON®M20 **NDA/ANDA#**

Established name, including dosage form:
Potassium Chloride Extended-release Tablets

Other trademarks by the same firm for companion products:

Please see attached note.

Indications for Use (may be a summary if proposed statement is lengthy):
[redacted] potassium replacement for prevention and/or correction of potassium deficit.

Initial Comments from the submitter (concerns, observations, etc.):

Please see attached note.

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

Rev. December 95 x:\wpfile\label\labeling.lnc

TO: CDER Labeling and Nomenclature Committee

FROM: Office of Generic Drugs, Labeling Review Branch

Upsher-Smith has proposed, "Klor-Con®M20", as a proprietary name for their 20 mEq Potassium Chloride Extended-release Tablets, USP. Upsher-Smith already has several approved potassium chloride drug products on the market that uses "Klor-Con" as part of the proprietary name. However, the dosage forms are in a powder[Klor-Con/25], an effervescent tablet [Klor-Con/EF] and a controlled-released tablet with a wax matrix [Klor-Con-10]. Their "Klor-Con®M20" product is a tablet formulation (not enteric coated or wax matrix) containing individually microencapsulated potassium chloride crystals which disperse upon tablet disintegration.

Does the committee find the proposed name acceptable?

Consult #635 (HFD-613)

KLOR-CON M20 potassium chloride extended-release tablets

Since Klor-Con is in the name of several marketed products, the Committee considered the acceptability of the suffix "M20". The Committee notes that the suffix stands for "20 mEq microencapsulated", and believes this is a meaningful modifier that would differentiate this product from the other Klor-Con products.

The Committee has no reason to find the proposed name unacceptable.

/S/ 8/1/96, Chair
CDER Labeling and Nomenclature Committee

TENTATIVE APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

Date of Review: July 22, 1996

Date of Submission: July 2, 1996

Primary Reviewer: Jacqueline White, Pharm.D.

ANDA Number: 74-726 Review Cycle: 2nd [FPL]

Applicant's Name [as seen on 356(h)]:
Upsher-Smith Laboratories, Inc.

Manufacturer's Name (If different than applicant):

Established Name: Potassium Chloride Extended-release Tablets, USP 20 mEq

---

NOTE TO THE CHEMSIT

The inactive ingredients listed in the DESCRIPTION section differ slightly from the innovator. Are they acceptable? OK

7/26

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes
If no, list why:

Container Labels: Satisfactory in FPL as of 7/2/96 submission- 100's, 500's & 1000's

Carton Labeling: n/a

Unit Dose Blister Label: Satisfactory in FPL as of 7/2/96 submission.

Unit Dose Carton Label: Satisfactory in FPL as of 7/2/96 submission-unit dose 100's.

Professional Package Insert Labeling: Satisfactory in FPL as of 7/2/96 submission.

Patient Package Insert Labeling: n/a

Auxiliary Labeling: n/a

Revisions needed post-approval:
DOSAGE AND ADMINISTRATION-
Paragraph 3: ... extended-release tablet provides ...
[Add "extended-release"].

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Kdur

NDA Number: 19-439

NDA Drug Name: Kdur (potassium chloride)

NDA Firm: Schering-Plough Research

Date of Approval of NDA Insert and supplement#:
NDA 19439 - S-015, approved 12/20/90

Has this been verified by the MIS system for the NDA?
Yes

Was this approval based upon an OGD labeling guidance?
No

If yes, give date of labeling guidance:

Basis of Approval for the Container Labels:Satisfactory in FPL as of 7/2/96 submission-unit dose 100's.

Basis of Approval for the Carton Labeling: Satisfactory in FPL as of 7/2/96 submission-unit dose 100's.

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	x		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			x

Error Prevention Analysis			
PROPRIETARY NAME			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		x	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in the FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product? [Individual cartons are required for UNIT DOSE packaging].			
Are there any other safety concerns?		x	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Error Prevention Analysis: *LABELING* (Continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)			x
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	

Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		x	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?.		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?	x		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? [See comment under DESCRIPTON].		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? [See FTR].		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling. [See FTR].	x		
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) [pending]			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. MODEL:

   Insert - KDur by Key Pharmaceuticals Inc. (Schering-Plough Research) [Revised 4/90 & Approved 12/20/90].

2. INACTIVE INGREDIENTS:

The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's composition statement [Vol. 1.12, p.3472].

3. SCORING:

RLD - scored
ANDA- Scored
[Description of the finished dosage form; Vol. 1.14, p.4576, 4621, 4867 & 4898].

[See comment under NOTE TO THE CHEMIST from review#1]

4. PACKAGING:

RLD - 100's, 500's, 1000's & unit dose 100's
ANDA- 100's, 500's, 1000's & unit dose 100's

5. USP ISSUES

The Description and Solubility of the product differs slightly from the USP. However, it is consistent with the RLD.

6. STORAGE recommendations:

USP- Preserve in tight containers
RLD-Insert: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).
Container: Store at controlled room temperature 15-30°C(59-86°F).
ANDA-Insert: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).
Container: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).

7. DISPENSING RECOMMENDATIONS:

USP- Dispense in tight containers
RLD- Insert: none
ANDA- Insert: None.
Container: Dispense in tight light-resistant container as defined in the USP.

8. PATENT AND EXCLUSIVITY:

KDur:
-Patent, "for use" [U-99; Method of providing potassium to a subject in need of potassium] expires 9/5/06 [16th.ed.]
-No exclusivity's pending

-The firm's patent certification statement of 9/22/95 [that indicates that no patent was pending] was addressed in our 8/28/95 correspondence. Upsher-Smith Laboratories, Inc. plans to notify Key Pharmaceuticals, holder of the approved listed drug, KDur, of patent non-infringement. See letter from firm dated 9/11/95.

9. CLOSURE:

ANDA: 100's - CRC
500's & 1000's - **non** child-resistant caps
100's unit dose - **non** child-resistant, with polyvinyl chloride & foil backing
[Vol. 1.14, p. 4369].

10. PROPRIETARY NAME

The firm's proposed proprietary name is "Klor-Con®M20". Upsher-Smith already has several potassium chloride drug products on the market that use "Klor-Con" as part of the proprietary name.

11. Following the manufactured by statement, the firm has the statement, "Certain manufacturing operations have been performed by other firms". [This is acceptable; CRF 21 201.1(C)(1).

12. ACCEPTABLE DIFFERENCES and/or DIFFERENCES IN THE LABELING OF ANDA vs. THE LABELING GUIDANCE

a. We have requested the firm to use the term "extended-release rather than "controlled release" or "sustained release". This differs from the Labeling Guidance.

- The innovator uses, "controlled release" or "sustained release"

b. CONTRAINDICATIONS

The last sentence of the second paragraph, includes product specific text for this ANDA, i.e., ... an aqueous (water) suspension ...".

- The innovator uses the same text.

c. PRECAUTIONS

i. Information for Patients:

A) There is text in this subsection that is product specific and refers to how to take the medication.

- This text is the same as the innovator.

B) The following paragraph is in the labeling guidance but not in the ANDA's labeling.

To check with the physician if there is trouble swallowing [tablets/capsules] or if the [tablets/capsules] seem to stick in the throat.

- This text is also missing from the innovator's labeling.

ii. DOSAGE AND ADMINISTRATION

a. Paragraph 3 -

Each Klor-Con®M20 extended-release tablet provides 1500 mg of potassium chloride and 20 mEq potassium.

- This text differs both from the labeling guidance and the innovator's labeling.

b. There is text in this section that is product specific and refers to instructions for administering the medication. [It is the same text found under Information for Patients].

13. Upsher Uspher uses the phrase "Micro-Dispersible Technology™" in their title and the innovator, KDur by Key Pharmaceuticals, Inc. uses the phrase "Microburst Release System". Both firms have the same description of their tablet release and tablet formulation in the DESCRIPTION secton.

14. The DOSAGE AND ADMINISTRATION section of the innovator's labeling & the ANDA's labeling indicate the following.

The fourth paragraph indicates that the drug product can be taken with a glass of water or other liquid. The last paragraph instructs that the use of other liquids for suspending Klor-Con®M20 tablets is <u>not</u> recommended.

Note: The first administration instructions refer to swallowing the tablet whole, and the later refers to using the tablet to prepare an aqueous suspension.

15. The Bio. reviewer has been informed [via E-mail] that the firm has included in their DOSAGE AND ADMINISTRATION section a statement that their extended-release tablet can be broken in half.

/S/ for 8/7/96

Primary Reviewer Date

/S/ 8/7/96

Acting Team Leader, Labeling Review Branch Date

cc: ANDA 74-726
Division File
HFD-613\JWhite\AVezza (no cc)

Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

Date of Review: March 5, 1996

Date of Submission: October 12, 1995 [Draft insert labeling]
August 8, 1995 [Draft container labels]

Primary Reviewer: Jacqueline White, Pharm.D.

ANDA Number: 74-726 Review Cycle: 1st[Draft]

Applicant's Name [as seen on 356(h)]: Upsher-Smith Laboratories, Inc.

Manufacturer's Name (If different than applicant):

Established Name: Potassium Chloride Extended-release Tablets, USP 20 mEq

LABELING DEFICIENCIES, WHICH ARE TO BE INCORPORATED WITH THE CHEMISTRY COMMENTS TO THE FIRM:

[NOTE: These deficiencies can be located on the x-drive as detailed in notes from Ted Sherwood regarding the New X-Drive]

A. CHEMISTRY DEFICIENCIES

B. LABELING DEFICIENCIES

1. CONTAINER:

a. 100's, 500's and 1000's

i. Front Panel

Revise "20 mEq" to read "20 mEq K".

ii. Side Panel

Each ... 1500 mg potassium chloride equivalent to (20 mEq of potassium).

b. Unit-Dose blister

Satisfactory in draft.

2. CARTON: Unit-Dose 100's

a. See comments under Container.

b. Include a statement as to whether or not the unit-dose package is child-resistant. If it is not child-resistant, we encourage the inclusion of a statement that if dispensed to outpatients, it should be with a child resistant container. For example:

This unit-dose package is not child-resistant. If dispensed for outpatient use, a child-resistant container should be utilized.
[Note: The second sentence is optional].

3. INSERT

a. GENERAL COMMENTS

i. Your proposed proprietary name "Klor-Con®M20" will be forwarded to the CDER Labeling and Nomenclature Committee for review and comment. We defer final comment on your proposed proprietary name pending notification of the committee's findings.

ii. Throughout the text of the insert use the term "extended-release rather than "controlled release" or "sustained release".

b. DESCRIPTION

Include the molecular weight, 74.55.

c. PRECAUTIONS

i. General

Use italic print for "*per se*".
[two places]

ii. Drug Interactions

Use italic print for "*in vitro*".

iii. Pregnancy

Please note "*Pregnancy*" is the subsection heading. Revise to read:

Pregnancy: Pregnancy Category C: Animal reproduction ...

iv. Pediatric Use

... pediatric patients have not ...

d. OVERDOSAGE

... dextrose injection containing ...
[replace "solution" with "injection"]

e. DOSAGE AND ADMINISTRATION

i. Paragraph 3 -

Each Klor-Con®M20 extended-release table provides 1500 mg of potassium chloride and 20 mEq potassium.

ii. Last paragraph -

... Klor-Con®M20 extended-release tablet that is not ...

f. HOW SUPPLIED

Is this an issue? Is it with this product or are there other types of scoring?

i. Please further describe the scoring of your tablet by indicating the type of score.

correction x-ref to 8 on 3/14/96

ii. Klor-Con®M20 Extended-release tablets, 1500 mg of potassium chloride (20 mEq of potassium) are ...

Please revise your labels and labeling, as instructed above, and submit in final print. Please note that we reserve the right to request further changes in your labels and labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

NOTE TO THE CHEMIST:

1. Has the firm described the type of score of their product, i.e., bisected? [See comment under HOW SUPPLIED]. See Chem rev. dec 3-26-96

2. Has the firm accurately described their tablet imprint, "USL 20"? [I was unable to locate this information in Description of the finished dosage form; Vol. 1.14, p.4576, 4621, 4867 & 4898]. See chem rev. dec 3-26-96

3. The firm's description of their tablet is not consistent with their description in the finished dosage form. Do you concur? [See comment under HOW SUPPLIED]. Is this what was meant? See Chem rev. dec 3-26-96

4. Do Upsher's tablets contain "individually microencapsulated potassium chloride crystals" and is the description of their tablet formulation in fourth paragraph of the DESCRIPTION section accurate? See Chem rev. dec 3-26-96

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes No

If no, list why:

Container Labels:

Carton Labeling:

Unit Dose Blister Label:

Unit Dose Carton Label:

Professional Package Insert Labeling:

Patient Package Insert Labeling:

Auxiliary Labeling:

Revisions needed post-approval:

BASIS OF APPROVAL:

Was this approval based upon a petition? Yes No

What is the RLD on the 356(h) form:

NDA Number:

NDA Drug Name:

NDA Firm:

Date of Approval of NDA Insert and supplement #:
Has this been verified by the MIS system for the NDA?
Yes No

Was this approval based upon an OGD labeling guidance?
Yes No

If yes, give date of labeling guidance:

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Applicant's Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	

Is this product a USP item? If so, USP supplement in which verification was assured. USP 23	x		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
PROPRIETARY NAME			
Has the firm proposed a proprietary name? If yes, complete this subsection.	x		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		x	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?		x	
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in the FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?			
Are there any other safety concerns?		x	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Error Prevention Analysis: *LABELING* (Continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)			x

Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		x	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		x	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?	x		
Has the firm failed to describe the scoring in the HOW SUPPLIED section?.		x	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?	x		
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?			x
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray? [See comment under DESCRIPTON].		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		x	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container? [See FTR].		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			x
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable) [pending]			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	

Patent/Exclusivity Issues: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. MODEL:

   Insert - KDur by Key Pharmaceuticals Inc. [Revised 4/90 & Approved 12/20/90].

2. INACTIVE INGREDIENTS:

   The inactive ingredients listed in the DESCRIPTION section are consistent with the firm's composition statement [Vol. 1.12, p.3472].

3. SCORING:

   RLD - scored
   ANDA- Scored
   [Description of the finished dosage form; Vol. 1.14, p.4576, 4621, 4867 & 4898].

   See comment under HOW SUPPLIED & NOTE TO THE CHEMIST.

4. PACKAGING:

   RLD - 100's, 500's, 1000's & unit dose 100's
   ANDA- 100's, 500's, 1000's & unit dose 100's

5. USP ISSUES

   The Description and Solubility of the product differs slightly from the USP. However, it is consistent with the RLD.

6. STORAGE recommendations:

   USP- Preserve in tight containers
   RLD-Insert: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).
   Container: Store at controlled room temperature 15-30°C(59-86°F).
   ANDA-Insert: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).
   Container: Keep tightly closed. Store at controlled room temperature 15-30°C(59-86°F).

7. DISPENSING RECOMMENDATIONS:

USP- Dispense in tight containers
RLD- Insert: none
ANDA- Insert: None.
Container: Dispense in tight light-resistant container as defined in the USP.

8. PATENT AND EXCLUSIVITY:

KDur:
-Patent, "for use" [U-99; Method of providing potassium to a subject in need of potassium] expires 9/5/06 [15th.ed.]
-No exclusivity's pending

-The firm's patent certification statement of 9/22/95 [that indicates that no patent was pending] was addressed in our 8/28/95 correspondence. Upsher-Smith Laboratories, Inc. plans to notify Key Pharmaceuticals, holder of the approved listed drug, KDur, of patent non-infringement. See letter from firm dated 9/11/95.

9. CLOSURE:

ANDA: 100's - CRC
500's & 1000's - **non**child-resistant caps
100's unit dose - **non**child-resistant, with polyvinyl chloride & foil backing
[Vol. 1.14, p. 4369].

10. PROPRIETARY NAME

The firm's proposed the proprietary name is "Klor-Con®M20". Upsher-Smith already has several potassium chloride drug products on the market that uses "Klor-Con" as part of the proprietary name.

11. Following the manufactured by statement, the firm has the statement, "Certain manufacturing operations have been performed by other firms". [This is acceptable; CRF 21 201.1(C)(1).

12. ACCEPTABLE DIFFERENCES IN THE LABELING OF ANDA vs. THE LABELING GUIDANCE

a. We have requested the firm to use the term "extended-release rather than "controlled release" or "sustained release". This differs from the Labeling Guidance.

- The innovator uses, "controlled release" or "sustained release"

b. CONTRAINDICATIONS

The last sentence of the second paragraph, includes product specific text for this ANDA, i.e., ... an aqueous (water) suspension ...".

- The innovator uses the same text.

c. PRECAUTIONS

i. Information for Patients:

A) There is text in this subsection that is product specific and refers to how to take the medication.

- This text is the same as the innovator.

B) The following paragraph is in the labeling guidance but not in the ANDA's labeling.

NOTE: This product is K-Dur please check what to do in this situation

To check with the physician if their is trouble swallowing [tablets/capsules] or if the [tablets/capsules] seem to stick in the throat.

- This text is also missing from the innovator's labeling. - K-DUR

ii. DOSAGE AND ADMINISTRATION

a. Paragraph 3 -

Each Klor-Con®M20 extended-release tablet provides 1500 mg of potassium chloride and 20 mEq potassium.

- This text differs both from the labeling guidance and the innovator's labeling.

b. There is text in this section that is product specific and refers instructs for administering the medication. [It is the same text found under Information for Patients].

13. Uspher uses the phrase "Micro-Dispersible Technology™" in their title and the innovator, KDur by Key Pharmaceuticals,

Inc. uses the phrase "Microburst Release System". Both firms have the same description of their tablet release and tablet formulation in the DESCRIPTION secton.

14. The DOSAGE AND ADMINISTRATION section of the innovator's labeling & the ANDA's labeling indicate the following.

> The fourth paragraph indicates that the drug product can be taken with a glass of water or other liquid. The last paragraph instructs that the use of other liquids for suspending Klor-Con®M20 tablets is <u>not</u> recommended.

Note: The first administration instructions refer to swallowing the tablet whole, and the later refers to using the tablet to prepare an aqueous suspension.

15. The Bio. reviewer has been informed [via E-mail] that the firm has included in their DOSAGE AND ADMINISTRATION section a statement that their extended-release tablet can be broken in half.

/S/ — 3-15-96

Primary Reviewer — Date

/S/ — 3-18-96

Team Leader, Labeling Review Branch — Date

cc: ANDA 74-726
Dup/Division File
HFD-613/JWhite/JGrace (no cc:)
HFD-600/RF

3/18/96

Review